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U.S. PATENT & TRADEMARK OFFICE

TRANSMITTAL OF APPEAL BRIEF (Small Entity)

Docket No.

In Re Application Of:

PUGLIESE, PETER T.

Serial No.

09/989,019

Filing Date

Nov. 21, 2001

Examiner

R.Travers/San-Ming Hui

Group Art Unit

1617

Invention:

THE USE OF COMBINED FLAVONES & ISOFLAVONES TO TREAT CELLULITE

TO THE ASSISTANT COMMISSIONER FOR PATENTS:

Transmitted herewith in triplicate is the Appeal Brief in this application, with respect to the Notice of Appeal filed on:

Applicant is a small entity under 37 CFR 1.9 and 1.27. Yes. (Of record)

A verified statement of small entity status under 37 CFR 1.27: No longer required by Rule

☐ is enclosed.

☒ has already been filed in this application.

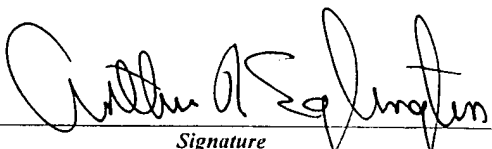
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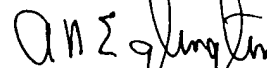
Dated:

1 February 2003

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Reg.#19,838

I certify that this document and fee is being deposited on 1 Feb 2003 with the U.S. Postal Service as first class mail under 37 C.F.R. 1.8 and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.



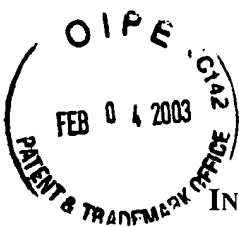
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A. R. EGLINGTON, ESQ

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT EXAMINING OPERATION

In re Application of:

PETER T. PUGLIESE

Serial No.: 09/989,019

Filed: November 21, 2001

Title: THE USE OF COMBINED FLAVONES
AND ISOFLAVONES TO TREAT
CELLULITE

Group Art Unit No.: 1617

Supervisory Examiner:

R. Travers (GP 1200)

Phone No.: (703) 308-3627

Examiner: San-Ming Hui

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**MAIN BRIEF TO THE BOARD OF APPEALS CONFORMING
WITH 37 C.F.R. §1.192(c) AS AMENDED 1995**

Sirs:

PREAMBLE

This appeal brief (filed in triplicate with a statutory fee) is being mailed on or about February 1, 2003, and is responsive to the Final Action of the Primary Examiner, mailed 09/10/2002, with a shortened statutory period for our response of three months. Appellant filed a short Rule 116 response on October 3, 2002, rebutting views taken by the Examiner as to the Specification support for certain claims, and concurrently tendering limiting amendments to one claim (#11) of the finally rejected set of claims.

In reply to the PTO Final Action mailed 09/10/02, the Appellant filed the mentioned brief R116 paper, rectifying an informality as to dependent Claim 11, for purposes of claims resolution on appeal. This step called for an advisory action from the PTO as to the tendered claim amendment. Such a PTO advisory has not yet been received, so our submission stands

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without objection. Thusly, amended claims form the sole appendix to this Brief on Appeal, reflect the new submission. Also, the of record Rule 132 Declaration of inventor, P.T. Pugliese, forms an integral part of this record on appeal.

This reply settled that the Notice of Appeal due date remained at December 10, 2002. A timely Notice of Appeal was entered on December 10, 2002. The statutory fee is enclosed.

REAL PARTY IN INTEREST

The of-record sole Applicant, Peter T. Pugliese, Pugliese Group, 4408-B Pottsville Pike, Reading, PA 19605, is the sole party in interest.

RELATED APPEALS AND INTERFERENCES

None.

STATUS OF CLAIMS ON APPEAL

None of the 11 claims are being represented in a continuation application hereof. Claims 1 to 11 inclusive, as amended remain on appeal.

STATUS OF AMENDMENTS

Appellant, based on the initial rejection of the Primary Examiner, had tendered a number of limiting and somewhat clarifying amendments to the once amended set of claims. Later suggested amendments were tendered pursuant to 27 C.F.R. § 1.116. The present brief and argumentation is focused on the amended claim set which form a major predicate of this brief.

DISSERTATION ON THE RELEVANT STATUTORY AND CASE LAW PERTINENT

HERE

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In a 1999 decision of the CAFC, *In re: Dembiczak et al*, 175 Fed Rpt. 3d 994, 998, the Court set forth a cogent analysis of the law relating to §103, where reliance on multiple references is the basis of a PTO rejection of claims. The pertinent passages are reproduced below:

“Our analysis begins in the text of section 103 quoted above, with the phrase “at the time the invention was made.” For it is this phrase that guards against entry into the “tempting but forbidden zone of hindsight,” see *Loctite Corp. v. Ultraseal Ltd.*, F.2d 861, 873, 228 USPQ 90, 98 (Fed. Cir. 1985), overruled on other grounds by *Nobelpharma AB v. Implant Innovations, Inc.*, F.3d 1059, 46 USPQ2d 1097 (Fed. Cir. 1993), when analyzing the patentability of claims pursuant to that section. Measuring a claimed invention against the standard established by section 103 requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. See, e.g., *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 313 (Fed. Cir. 1983). Close adherence to this methodology is especially important in the case of less technologically complex inventions, where the very ease of which the invention can be understood may prompt one “to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.” *Id.*

Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. See, e.g., *C.R. Bards, Inc. v. M3 Sys., Inc.* 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998) (describing “teaching or suggestion or motivation [to combine]” as an “essential evidentiary component of an obviousness holding”); *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) (“the Board must identify specifically . . . the reasons one of ordinary skill in the art would have been motivated to select the references and combine them”); *In re Fritch*, 972 F.3d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (examiner can satisfy burden of obviousness in light of combination “only by showing some objective teaching [leading to the combination]”); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) (evidence of teaching or suggestion “essential” to avoid hindsight); *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 297, 227 USPQ 657, 667 (Fed. Cir. 1985) (district court’s conclusion of obviousness was error when it “did not elucidate any factual teachings, suggestions or incentives from this prior art that showed the propriety of combination”). See also *Graham*,

383 U.S. at 18, 86 S.Ct. 684, 15 L.Ed.2d 545, 148 USPQ at 467 (“strict observance” of factual predicates to obviousness conclusion required). Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor’s disclosure as a blueprint for piecing together the prior art to defeat patentability – the essence of hindsight. *See, e.g., Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed.Cir.1985) (“The invention must be viewed not with the blueprint drawn by the inventor, but in the state of art that existed at the time.”). In this case, the Board fell into the hindsight trap.

We have noted that evidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of the ordinary skill in the art, or, in some cases, from the nature of the problem to be solved, *see Pro-Mold & Tool Co., v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed.Cir. 1996), *Para-Ordnance Mfg. v. SGS Importers Intern., Inc.*, 73 F.3d 1085, 1088, 37 USPQ2d 1237, 1240 (Fed.Cir.1995), although “the suggestion more often comes from the teachings of the pertinent references,” *Rouffet*, 149 F.3d at 1355, 47 USPQ2d at 1456. The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular. *See, e.g., C.R. Bard*, 157 F.3d at 13532, 48 USPQ2d at 1232. Broad conclusory statements regarding the teaching of multiple references, standing alone, are not “evidence.” *E.G., McElmurry v. Arkansas Power & Light Co.*, 995 F.2d 1576, 1578, 27 USPQ2d 1129, 1131 (Fed.Cir.1993) (“Mere denials and conclusory statements, however, are not sufficient to establish a genuine issue of material fact.”); *In re Sichert*, 566 F.2d 1154, 1164, 196 USPQ 209, 217, (CCPA 1977) (“The examiner’s conclusory statement that the specification does not teach the best mode of using the invention is unaccompanied by evidence or reasoning and is entirely inadequate to support the rejection.”). In addition to demonstrating the propriety of an obviousness analysis, particular factual findings regarding the suggestion, teaching, or motivation to combine serve a number of important purposes, including: (1) clear explication of the position adopted by the Examiner and the Boards; (2) identification of the factual disputes, if any, between the applicant and the Board; and (3) facilitation of review on appeal. Here, however, the Board did not make particular findings regarding the locus of suggestion, teaching, or motivation to combine the prior art references.

All the obviousness rejections affirmed by the Board resulted from a combination of prior art references, e.g., the conventional trash or yard bags, and the Holiday and Shapiro publications teaching. . .”

* * *

Nor has the Primary Examiner followed the mandate of the CAFC in properly explicating the necessary factual findings so to provide an administrative record showing PTO “evidence”,

on which such findings are based.

A recent panel of the CAFC in *In re Sang-Su Ling* (18 2002) 277 Fed. Report 3d 1338/9, in reversing the BPAI, articulated the settled philosophy of that court on a crucial aspect of patent solicitation and an Examiner invocation of Section 103. In the interest of brevity, only four headnotes (3, 7, 8, and 9) are reproduced below (the full text of that decision is constructively available to the Primary Examiner, or will be supplied by Applicant upon informal request to counsel):

“3. Patents 113(6)

Judicial review of a decision of the Board of Patent Appeals and Interferences denying an application for patent is founded on the obligation of the agency to make the necessary findings and to provide an administrative record showing the evidence on which the findings are based, accompanied by the agency’s reasoning in reaching its conclusions. 5 U.S.C.A. § 103.

7. Patents 111

Analysis of invention by Board of Patent Appeals and Interferences did not comport with either legal requirements for determination of obviousness or with requirements of Administrative Procedure Act (APA) on basis that agency tribunal did not set forth findings and explanations needed for reasoned decisionmaking; examiner used conclusory statements to support this subjective belief that it was obvious that person skilled in the art would have been motivated to combine prior art, and Board rejected need for any specific hint or suggestion in particular reference to support combination of prior art. 5 U.S.C.A. § 706(2); 35 U.S.C.A. § 103.

8. Patents 26(1)

In an obviousness determination, the factual question of motivation to combine prior art is material to patentability, and cannot be resolved on subjective belief and unknown authority. 35 U.S.C.A. § 103.

9. Patents 26(1), 111

In an obviousness determination under patent law, it is improper, in determining whether a person of ordinary skill would have been led to combine references, simply to use that which the inventor taught against its teacher; thus, the Board of Patent Appeals and Interferences must not only assure that the requisite findings are made, based on evidence of record, but must also explain the reasoning by which the findings are deemed to support the agency’s conclusion. 5 U.S.C.A. §

705(2); 35 U.S.C.A. § 103.

SHIFT IN THE EVIDENTIARY BURDEN TO THE PTO PRIMARY EXAMINER

This specification recitation, coupled with the Rule 132 declaration of the sole inventor, has been untenably given short shrift by the Primary Examiner. While the §103 basis of rejection may have been arguable, the of record showings served to overcome any presumption of obviousness, so the final rejection of the invented claims is contrary to patent law standards of the 35 U.S. Code requirements as set forth in §101 and 103.

ARGUMENT REFUTING THE CLAIMS REJECTION PER §103

At the outset, the thrust of the present invention bears repeating. According to the present invention, a treatment protocol for the cosmetic condition in females, commonly known as cellulite, involves novel utilization of the following inter-related physiological precepts. Estrogen can be inhibited by blocking estrogen receptors (ER) located on the fibroblast cells with a selected isoflavone, like genistein. Collagen fibers form a tough fibrous tissue termed the fascia, which hold fatty tissues in discrete compartments. Collagenase breaks down collagen fibers. The action of collagenase can be blocked at the level of collagen by employing proanthocyanidins. The production of estrogen from testosterone can be blocked by another isoflavone like genistein. This isoflavone also blocks the initiation of preadipocytes by estrogen, to form fully-differentiated adipocytes, thus inhibiting the expansion of fat mass. Fat tissue may also be reduced by stimulating the formation of cyclic adenosine triphosphate (cAMP), which cause the activation of lipase on fatty tissue, with coleus forskohlii serving as an effective stimulator of cAMP. The xanthine and theophylline acetate, inhibit the enzymatic action of phosphodiesterase, which destroy a cAMP, thus prolonging the lipase stimulating action of

cAMP. Finally, a cofactor like acetyl carnitine is employed to increase the metabolism of the released free fatty acids by the mitochondria. The protocol is foreign to the citations.

The original 11 claims were rejected under Patent Code §103(a) based on a shotgun (varied) reliance on four U.S. patents Soudant, Majeed, Sekiya, and Koulbanis, two foreign patent documents (Lotte and DeSimone), and two non-patent documents (Kuppusamy and Gennaro), for a total of eight citations.

So, of the six primary citations relied upon by the PTO, only one, Koulbanis '433 even speaks to anti-cellulitis action. Of the two secondary citations, De Simone relates solely to the treatment of cytological disorders, while the Gennaro text teaches that methylcellulose and carrageen are useful jelling agents. So, neither of the secondary citations relate to the treatment of cellulite. The asserted merging of these teachings is classic prohibited hindsight reconstructions.

Broadly, the Examiner has asserted a hindsight reconstruction from scattered citations in seeking to effect a teaching or suggestion of the claimed multicomponent formulation of the present invention. The suggestion to combine elements found in the prior art must come from the Applicant himself, rejections born of hindsight are improper. *Panduit Corp. v. Dennison*, 774 Fed. 2d 1082, 1091-92, (CAFC 1985). It is basic patent law that if a prima facie obviousness, the teachings of references can be combined only if there is some suggestion or incentive to do so. (*ACS Hosp. Sys. v. Montefiore Hospital*, 732 Fd. 1572, 1577 (CAFC 1984).

Also, there must be some reason, suggestion, or motivation found in the prior art, whereby a person of ordinary skill in the field, would make that combination. *In re: Octiker*, 977 Fd. 1443, 1447) CAFC 1992).

In the PTO action of February 14, 2002, pages 3/4, the Examiner notes what elements are common to the present claims that the citations do teach or suggest. In that PTO Action page 4, she concedes that several of the recited elements in the examined claims are neither taught, or let alone suggested. The Applicant will now set forth what other features and motivations that each of the citations lack; and what law precludes the picking and choosing of elements for a proscribed force-fitting of these disparate references in striving to meet the here-claimed recitations.

Soudant '230 teaches a topical emulsion composition containing lipolytic agents, like caffeine and a carnitine, for "slimming." It makes neither a mention of, or suggestion for, use of an isoflavone, a hydroxyflavone, a plant extract that stimulates the action of cyclic AMP, any other bioflavanoids, or capillary protectants, all of which are presently taught and comprise components of the claimed formulation.

While Majeed '596 addresses a method of promoting lean body mass, and treating of a mood disorder by administering internally an effective amount of forskolin, it does not even recognize the distinct biological phenomenon of female cellulite. It surely does not suggest c. forskohlin for inclusion in any topical formulation for treating that cosmetic disorder in women. So there is no motivation or incentive provided here to consider forskoilii in the present setting.

While the Lotte Abstract speaks to lipase inhibitors, containing flavanoid compounds as active agents, to be used in food and drink, only quercetin of the hydroflavones is taught as useful, when combined with McIlvane buffer (a complex oleate and swine spleen lipase), for oral ingestion. Again, there is no mention of human cellulite, or any suggestion of possible utility in a topical, extended term treatment using this hydroxyflavone, inter alia, biochemical compounds.

The Kuppusamy article (1992) is directed to the effects of flavanoids on cyclic AMP and phosphodiesterase on lipids in rat adipocytes. It lists quercetin and fisetin among the 31 flavanoids tested. As to these two flavanoids, they showed a dose-and-time dependent increase in lipolysis which was synergistic with epinephrine. However, there is no teaching here of such flavanoids as being candidate compositions for topical treatment of cellulite, which includes an isoflavone, like genistein or diadzein; and acetyl, L-carnitine to move the fatty acids; a plant extract like coleus F; or other bioflavanoids as capillary protectants. The reference-cited hydroxyflavones are merely two species of the several compounds of the here claimed formulations. They are not remotely suggested for such an anti-cellulite evaluation by the Kuppusamy technical paper.

Sekiya '906 is directed to a method of promoting fat degradation in fat cells by orally, or by injection, of a selected isoflavone to a human subject. The basis for this is solely on in vitro data with preadipocyte (a fat cell precursor). While neither genistein, diadzin or daidzein, or diazeine were tested, and optional with customary inert additives, like bulky agents and excipients included, the selected isoflavones were to be used alone. There is neither a teaching or suggestion here of the use of a topical formulation wherein the hydroxyflavone, a xanthine derivative, and acetyl carnitine, a plant extract like c. Forskohli, and capillary protectant are combined into a useful composition for topical treatment of cellulite. Consequently, while Sekiya is related technology, it lacks any motivation to alter its precise isoflavones so as to be blended with the more complex formulations of the present invention.

Koulbanis '433 is to cosmetic compositions having in combination, a thioether, and a xanthine derivative, applied topically with massage, or by using trans-cutaneous electrophoresis.

The patent is exemplification is limited to caffeine and theophylline, as “an anti-cellulitis” solutions. No other active composition are taught or suggested. The patent is directed to massage or using transcutaneous electrophoresis. As to the “slimming” action, only example VII goes to that, but the recited “cream” formulation employs no enzymes or flavanoids, at all. Cellulitis is not mentioned.

The DeSimone PCT international patent specification teaches the use of L-acetyl carnitines, among other carnatines, for the treatment of cytological disorders related to IGF-I (insulin-like growth factor). This shotgun disclosure is directed to numerous pathologies (see claim 2 for a long list of them), with only obesity having the remotest connection to the female cellulite. Cellulite is, in fact, not mentioned. There is no suggestion of any other active principals, in fact, not of the isoflavones, hydroxyflavones, xanthine, plant extract, and so forth. The reference focuses solely on carnitine derivatives and in no way relates to the formulation of the present invention directed to treatment of cellulite

Lastly, the Examiner would invoke the Gennaro text for the proposition that methyl cellulose and carrageenan are useful as gelling agents, an observation with which Applicant does not take issue. The recitation of these inert ingredients in present dependent claim 9 is not presented as being an independent invention. Rather, it goes to reciting preferred formulations. It is statutory law that these dependent claims incorporate all of the recitations of the independent claims from which they depend.

By way of augmentation of the Specification, in teaching the testing of candidate active entities described in the formulas, a showing from this Applicant under 37 C.F.R. Section 1.68 and 1.132 was submitted. This showing comprises quantifiable clinical evidence that the leading

active components, like genistein, diadzein, and quercetin, when incorporated into topical emulsions will produce an appreciable reduction in fat infiltration, increase connective tissues, and will effect a cosmetic improvement in the appearance of the buttocks.

Looking again to the of-record evidence of Appellant, there is the undisputed recitation of Specification pages 12 and 13, also of the Rule 132 Declaration of P.T. Pugliese. From the bar charts of that Declaration, it is clear that the lead compound (genistein) is capable of inhibiting the undesirable destructive effects of estrogen on connective tissue. Genistein is representative of the three-member Markush Group of main Claim 1. Utility has been shown for this novel formulation. Unexpected results here are absolutely not called for under the patent statute.

The Examiner's allegation that it would have been obvious when the invention was made to employ all the active compounds together in one composition or method is simply untenable. Most of this citation is focused on narrowed human conditions, if at all, or teach only one or two active principles for a clinical effect. To meet even the terms of the oil-in-water emulsion of claim 1 for topical use, the Examiner has resorted to at least four different publications, each of which does not provide a motivation for it's dissection and reconstitution in a novel context.

Indeed, it can be argued that certain of these citations teach away from the present formulations, which thus undermines prima facie obviousness. Cf. *In re: Sponnable*, 405 Fd 2d 578, 587 (CCPA 1969). A reference teaches a way when a person of ordinary skill would be led in direction divergent from that of the path taken by the Applicant here.

By way of example, Soudant, Majeed, Lotte, Sekiya, and DeSimone are all directed to treatments for other human problems, like the varied manifestations of obesity. None, save

Koulbanis, even speak to anti-cellulitis action.*

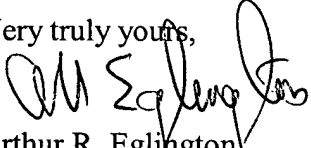
The contrived cutting and pasting of the several citations is untenable in the law, and should be withdrawn upon fresh reconsideration in light of these extended remarks.

Lastly, the enclosed Rule 132 Declaration establishes that representative flavones are capable of inhibiting the undesirable destructive effects of estrogen on connective tissue and thus provide a positive effect on treating cellulite, not cellulitis.

The allowance of the agreeably amended set of original claims 1-11, is courteously solicited.

Date: February , 2003
Appendix: All Claims on Appeal

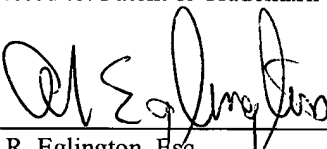
Very truly yours,


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CERTIFICATE OF MAILING

The undersigned hereby certifies that this MAIN BRIEF ON APPEAL TO THE BOARD CONFORMING WITH 37 C.F.R. §1.192(c) AS AMENDED correspondence is being deposited with the United States Postal Service as First Class Certified Mail in an envelope addressed to: Patent & Trademark Office, Attn: Group 3625, Washington, DC 20231, on February 1, 2003

Date: February 1, 2003



Arthur R. Eglington, Esq.

* Cellulitis is inflammation of cellular or connective tissues, which is not CELLULITE, as defined herein.
Taber's Medical Dictionary 1981 Ed. pg. 37.

APPENDIX CLEAN COPY OF CLAIMS

1. An oil-in-water emulsion suited for topical application to the skin of a woman evincing the cosmetic condition called cellulite, having the active ingredients comprising:

(a) an oil-soluble hydroxyflavone selected from the group consisted of quercetin and fisetin;

(b) an oil-soluble isoflavone selected from the group consisting of genistein, diadzein, and biochanin-A;

(c) an oil-soluble amino substituted butanoate selected from the group consisting of DL-carnitine, L-carnitine, and carnitine acetate;

(d) a water-soluble xanthine selected from the group consisting of theophylline, theophylline salts, caffeine, and theobromine;

(e) a water-soluble plant extract *coleus forskohlii*;

(f) a solubilizing agent for the oil-soluble ingredients; and,

(g) an emulsifying agent for mixing the oil phase with the aqueous phase.

2. The oil-in-water emulsion of Claim 1 wherein quercetin is the hydroxyflavone present in the weight percent of the emulsion volume up to about 5%.

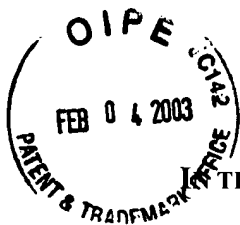
3. The oil-in-water emulsion of Claim 1 wherein fisetin is the hydroxyflavone and is present in the weight volume up to about 5%.

4. The oil-in-water emulsion of Claim 1 wherein the isoflavone is genistein and is present in the weight volume of up to about 5%.

5. The oil-in-water emulsion of Claim 1 wherein the xanthine is theophylline acetate and is present in the weight volume of up to about 4%.

6. The oil-in-water emulsion of Claim 1 wherein the coleus extract is present in the weight volume of up to about 2%.
7. The oil-in-water emulsion of Claim 1 wherein the butanoate is L-acetyl carnitine and is present in the weight volume of up to about 1.5%.
8. The method of treating cellulitis in women wherein the application formulation comprises an oil-in-water emulsion comprising:
 - (a) an oil-soluble hydroxyflavone selected from the group consisted of quercetin and fificetin;
 - (b) an oil-soluble isoflavone selected from the group consisting of genistein, diadzein, and biochanin-A;
 - (c) an oil-soluble amino substitute butanoate selected from the group consisting of DL-carnitine, L-carnitine, and carnitine acetate;
 - (d) a water-soluble xanthine selected from the group consisting of theophylline, theophylline salts, caffeine, and theopromine;
 - (e) a water-soluble plant extract coleus forskohlii;
 - (f) a solubizing agent for the oil-soluble ingredients; and,
 - (g) an emulsifying agent for mixing the oil phase with the aqueous phase.
9. The oil-in-water emulsion of Claim 1 which has been converted to a gel consistency by the incorporation of a natural gum selected from xanthan gum, and carrageenan.
10. The oil-in-water emulsion of Claim 1 which has been converted to a gel consistency by the incorporation of a gelling agent selected from one of methoxycellulose, ethoxycellulose, carboxycellulose, acyanacrylate, polyvinylpyrrolidine, or chitosan.

11. The oil-in-water emulsion of Claim 1 wherein the [bioflavonoid] oligomeric proanthrocyanidins are included as useful in blocking the action of collagenase.



THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT EXAMINING OPERATION

2 of 3

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PETER T. PUGLIESE

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without objection. Thusly, amended claims form the sole appendix to this Brief on Appeal, reflect the new submission. Also, the of record Rule 132 Declaration of inventor, P.T. Pugliese, forms an integral part of this record on appeal.

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None.

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None of the 11 claims are being represented in a continuation application hereof. Claims 1 to 11 inclusive, as amended remain on appeal.

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**DISSERTATION ON THE RELEVANT STATUTORY AND CASE LAW PERTINENT
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Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. See, e.g., *C.R. Bards, Inc. v. M3 Sys., Inc.* 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998) (describing “teaching or suggestion or motivation [to combine]” as an “essential evidentiary component of an obviousness holding”); *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) (“the Board must identify specifically . . . the reasons one of ordinary skill in the art would have been motivated to select the references and combine them”); *In re Fritch*, 972 F.3d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (examiner can satisfy burden of obviousness in light of combination “only by showing some objective teaching [leading to the combination]”); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) (evidence of teaching or suggestion “essential” to avoid hindsight); *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 297, 227 USPQ 657, 667 (Fed. Cir. 1985) (district court’s conclusion of obviousness was error when it “did not elucidate any factual teachings, suggestions or incentives from this prior art that showed the propriety of combination”). See also *Graham*,

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We have noted that evidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of the ordinary skill in the art, or, in some cases, from the nature of the problem to be solved, *see Pro-Mold & Tool Co., v. great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed.Cir. 1996), *Para-Ordnance Mfg. v. SGS Importers Intern., Inc.*, 73 F.3d 1085, 1088, 37 USPQ2d 1237, 1240 (Fed.Cir.1995), although “the suggestion more often comes from the teachings of the pertinent references,” *Rouffet*, 149 F.3d at 1355, 47 USPQ2d at 1456. The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular. *Se, e.g., C.R. Bard*, 157 F.3d at 13532, 48 USPQ2d at 1232. Broad conclusory statements regarding the teaching of multiple references, standing alone, are not “evidence.” *E.G., McElmurry v. Arkansas Power & Light co.*, 995 F.2d 1576, 1578, 27 USPQ2d 1129, 1131 (Fed.Cir.1993) (“Mere denials and conclusory statements, however, are not sufficient to establish a genuine issue of material fact.”): *In re Sichert*, 566 F.2d 1154, 1164, 196 USPQ 209, 217, (CCPA 1977) (“The examiner’s conclusory statement that the specification does not teach the best mode of using the invention is unaccompanied by evidence or reasoning and is entirely inadequate to support the rejection.”). In addition to demonstrating the propriety of an obviousness analysis, particular factual findings regarding the suggestion, teaching, or motivation to combine serve a number of important purposes, including: (1) clear explication of the position adopted by the Examiner and the Boards; (2) identification of the factual disputes, if any, between the applicant and the Board; and (3) facilitation of review on appeal. Here, however, the Board did not make particular findings regarding the locus of suggestion, teaching, or motivation to combine the prior art references.

All the obviousness rejections affirmed by the Board resulted from a combination of prior art references, e.g., the conventional trash or yard bags, and the Holiday and Shapiro publications teaching. . .”

* * *

Nor has the Primary Examiner followed the mandate of the CAFC in properly explicating the necessary factual findings so to provide an administrative record showing PTO “evidence”,

on which such findings are based.

A recent panel of the CAFC in *In re Sang-Su Ling* (18 2002) 277 Fed. Report 3d 1338/9, in reversing the BPAI, articulated the settled philosophy of that court on a crucial aspect of patent solicitation and an Examiner invocation of Section 103. In the interest of brevity, only four headnotes (3, 7, 8, and 9) are reproduced below (the full text of that decision is constructively available to the Primary Examiner, or will be supplied by Applicant upon informal request to counsel):

“3. Patents 113(6)

Judicial review of a decision of the Board of Patent Appeals and Interferences denying an application for patent is founded on the obligation of the agency to make the necessary findings and to provide an administrative record showing the evidence on which the findings are based, accompanied by the agency’s reasoning in reaching its conclusions. 5 U.S.C.A. § 103.

7. Patents 111

Analysis of invention by Board of Patent Appeals and Interferences did not comport with either legal requirements for determination of obviousness or with requirements of Administrative Procedure Act (APA) on basis that agency tribunal did not set forth findings and explanations needed for reasoned decisionmaking; examiner used conclusory statements to support this subjective belief that it was obvious that person skilled in the art would have been motivated to combine prior art, and Board rejected need for any specific hint or suggestion in particular reference to support combination of prior art. 5 U.S.C.A. § 706(2); 35 U.S.C.A. § 103.

8. Patents 26(1)

In an obviousness determination, the factual question of motivation to combine prior art is material to patentability, and cannot be resolved on subjective belief and unknown authority. 35 U.S.C.A. § 103.

9. Patents 26(1), 111

In an obviousness determination under patent law, it is improper, in determining whether a person of ordinary skill would have been led to combine references, simply to use that which the inventor taught against its teacher; thus, the Board of Patent Appeals and Interferences must not only assure that the requisite findings are made, based on evidence of record, but must also explain the reasoning by which the findings are deemed to support the agency’s conclusion. 5 U.S.C.A. §

705(2); 35 U.S.C.A. § 103.

SHIFT IN THE EVIDENTIARY BURDEN TO THE PTO PRIMARY EXAMINER

This specification recitation, coupled with the Rule 132 declaration of the sole inventor, has been untenably given short shrift by the Primary Examiner. While the §103 basis of rejection may have been arguable, the of record showings served to overcome any presumption of obviousness, so the final rejection of the invented claims is contrary to patent law standards of the 35 U.S. Code requirements as set forth in §101 and 103.

ARGUMENT REFUTING THE CLAIMS REJECTION PER §103

At the outset, the thrust of the present invention bears repeating. According to the present invention, a treatment protocol for the cosmetic condition in females, commonly known as cellulite, involves novel utilization of the following inter-related physiological precepts. Estrogen can be inhibited by blocking estrogen receptors (ER) located on the fibroblast cells with a selected isoflavone, like genistein. Collagen fibers form a tough fibrous tissue termed the fascia, which hold fatty tissues in discrete compartments. Collagenase breaks down collagen fibers. The action of collagenase can be blocked at the level of collagen by employing proanthocyanidins. The production of estrogen from testosterone can be blocked by another isoflavone like genistein. This isoflavone also blocks the initiation of preadipocytes by estrogen, to form fully-differentiated adipocytes, thus inhibiting the expansion of fat mass. Fat tissue may also be reduced by stimulating the formation of cyclic adenosine triphosphate (cAMP), which cause the activation of lipase on fatty tissue, with coleus forskohlii serving as an effective stimulator of cAMP. The xanthine and theophylline acetate, inhibit the enzymatic action of phosphodiesterase, which destroy a cAMP, thus prolonging the lipase stimulating action of

cAMP. Finally, a cofactor like acetyl carnitine is employed to increase the metabolism of the released free fatty acids by the mitochondria. The protocol is foreign to the citations.

The original 11 claims were rejected under Patent Code §103(a) based on a shotgun (varied) reliance on four U.S. patents Soudant, Majeed, Sekiya, and Koulbanis, two foreign patent documents (Lotte and DeSimone), and two non-patent documents (Kuppusamy and Gennaro), for a total of eight citations.

So, of the six primary citations relied upon by the PTO, only one, Koulbanis '433 even speaks to anti-cellulitis action. Of the two secondary citations, De Simone relates solely to the treatment of cytological disorders, while the Gennaro text teaches that methylcellulose and carrageen are useful jelling agents. So, neither of the secondary citations relate to the treatment of cellulite. The asserted merging of these teachings is classic prohibited hindsight reconstructions.

Broadly, the Examiner has asserted a hindsight reconstruction from scattered citations in seeking to effect a teaching or suggestion of the claimed multicomponent formulation of the present invention. The suggestion to combine elements found in the prior art must come from the Applicant himself, rejections born of hindsight are improper. *Panduit Corp. v. Dennison*, 774 Fed. 2d 1082, 1091-92, (CAFC 1985). It is basic patent law that if a prima facie obviousness, the teachings of references can be combined only if there is some suggestion or incentive to do so. (*ACS Hosp. Sys. v. Montefiore Hospital*, 732 Fd. 1572, 1577 (CAFC 1984).

Also, there must be some reason, suggestion, or motivation found in the prior art, whereby a person of ordinary skill in the field, would make that combination. In re: *Octiker*, 977 Fd. 1443, 1447) CAFC 1992).

In the PTO action of February 14, 2002, pages 3/4, the Examiner notes what elements are common to the present claims that the citations do teach or suggest. In that PTO Action page 4, she concedes that several of the recited elements in the examined claims are neither taught, or let alone suggested. The Applicant will now set forth what other features and motivations that each of the citations lack; and what law precludes the picking and choosing of elements for a proscribed force-fitting of these disparate references in striving to meet the here-claimed recitations.

Soudant '230 teaches a topical emulsion composition containing lipolytic agents, like caffeine and a carnitine, for "slimming." It makes neither a mention of, or suggestion for, use of an isoflavone, a hydroxyflavone, a plant extract that stimulates the action of cyclic AMP, any other bioflavanoids, or capillary protectants, all of which are presently taught and comprise components of the claimed formulation.

While Majeed '596 addresses a method of promoting lean body mass, and treating of a mood disorder by administering internally an effective amount of forskolin, it does not even recognize the distinct biological phenomenon of female cellulite. It surely does not suggest c. forskohlin for inclusion in any topical formulation for treating that cosmetic disorder in women. So there is no motivation or incentive provided here to consider forskoilii in the present setting.

While the Lotte Abstract speaks to lipase inhibitors, containing flavanoid compounds as active agents, to be used in food and drink, only quercetin of the hydroflavones is taught as useful, when combined with McIlvane buffer (a complex oleate and swine spleen lipase), for oral ingestion. Again, there is no mention of human cellulite, or any suggestion of possible utility in a topical, extended term treatment using this hydroxyflavone, inter alia, biochemical compounds.

The Kuppusamy article (1992) is directed to the effects of flavanoids on cyclic AMP and phosphodiesterase on lipids in rat adipocytes. It lists quercetin and fisetin among the 31 flavanoids tested. As to these two flavanoids, they showed a dose-and-time dependent increase in lipolysis which was synergistic with epinephrine. However, there is no teaching here of such flavanoids as being candidate compositions for topical treatment of cellulite, which includes an isoflavone, like genistein or diadzein; and acetyl, L-carnitine to move the fatty acids; a plant extract like coleus F; or other bioflavanoids as capillary protectants. The reference-cited hydroxyflavones are merely two species of the several compounds of the here claimed formulations. They are not remotely suggested for such an anti-cellulite evaluation by the Kuppusamy technical paper.

Sekiya '906 is directed to a method of promoting fat degradation in fat cells by orally, or by injection, of a selected isoflavone to a human subject. The basis for this is solely on in vitro data with preadipocyte (a fat cell precursor). While neither genistein, diadzin or daidzein, or diazeine were tested, and optional with customary inert additives, like bulky agents and excipients included, the selected isoflavones were to be used alone. There is neither a teaching or suggestion here of the use of a topical formulation wherein the hydroxyflavone, a xanthine derivative, and acetyl carnitine, a plant extract like c. Forskohli, and capillary protectant are combined into a useful composition for topical treatment of cellulite. Consequently, while Sekiya is related technology, it lacks any motivation to alter its precise isoflavones so as to be blended with the more complex formulations of the present invention.

Koulbanis '433 is to cosmetic compositions having in combination, a thioether, and a xanthine derivative, applied topically with massage, or by using trans-cutaneous electrophoresis.

The patent is exemplification is limited to caffeine and theophylline, as “an anti-cellulitis” solutions. No other active composition are taught or suggested. The patent is directed to massage or using transcutaneous electrophoresis. As to the “slimming” action, only example VII goes to that, but the recited “cream” formulation employs no enzymes or flavanoids, at all. Cellulitis is not mentioned.

The DeSimone PCT international patent specification teaches the use of L-acetyl carnitines, among other carnitines, for the treatment of cytological disorders related to IGF-I (insulin-like growth factor). This shotgun disclosure is directed to numerous pathologies (see claim 2 for a long list of them), with only obesity having the remotest connection to the female cellulite. Cellulite is, in fact, not mentioned. There is no suggestion of any other active principals, in fact, not of the isoflavones, hydroxyflavones, xanthine, plant extract, and so forth. The reference focuses solely on carnitine derivatives and in no way relates to the formulation of the present invention directed to treatment of cellulite

Lastly, the Examiner would invoke the Gennaro text for the proposition that methyl cellulose and carrageenan are useful as gelling agents, an observation with which Applicant does not take issue. The recitation of these inert ingredients in present dependent claim 9 is not presented as being an independent invention. Rather, it goes to reciting preferred formulations. It is statutory law that these dependent claims incorporate all of the recitations of the independent claims from which they depend.

By way of augmentation of the Specification, in teaching the testing of candidate active entities described in the formulas, a showing from this Applicant under 37 C.F.R. Section 1.68 and 1.132 was submitted. This showing comprises quantifiable clinical evidence that the leading

active components, like genistein, diadzein, and quercetin, when incorporated into topical emulsions will produce an appreciable reduction in fat infiltration, increase connective tissues, and will effect a cosmetic improvement in the appearance of the buttocks.

Looking again to the of-record evidence of Appellant, there is the undisputed recitation of Specification pages 12 and 13, also of the Rule 132 Declaration of P.T. Pugliese. From the bar charts of that Declaration, it is clear that the lead compound (genistein) is capable of inhibiting the undesirable destructive effects of estrogen on connective tissue. Genistein is representative of the three-member Markush Group of main Claim 1. Utility has been shown for this novel formulation. Unexpected results here are absolutely not called for under the patent statute.

The Examiner's allegation that it would have been obvious when the invention was made to employ all the active compounds together in one composition or method is simply untenable. Most of this citation is focused on narrowed human conditions, if at all, or teach only one or two active principles for a clinical effect. To meet even the terms of the oil-in-water emulsion of claim 1 for topical use, the Examiner has resorted to at least four different publications, each of which does not provide a motivation for its dissection and reconstitution in a novel context.

Indeed, it can be argued that certain of these citations teach away from the present formulations, which thus undermines prima facie obviousness. Cf. *In re: Spinnable*, 405 Fd 2d 578, 587 (CCPA 1969). A reference teaches a way when a person of ordinary skill would be led in direction divergent from that of the path taken by the Applicant here.

By way of example, Soudant, Majeed, Lotte, Sekiya, and DeSimone are all directed to treatments for other human problems, like the varied manifestations of obesity. None, save

Koulbanis, even speak to anti-cellulitis action.*

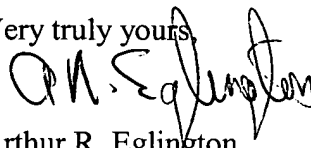
The contrived cutting and pasting of the several citations is untenable in the law, and should be withdrawn upon fresh reconsideration in light of these extended remarks.

Lastly, the enclosed Rule 132 Declaration establishes that representative flavones are capable of inhibiting the undesirable destructive effects of estrogen on connective tissue and thus provide a positive effect on treating cellulite, not cellulitis.

The allowance of the agreeably amended set of original claims 1-11, is courteously solicited.

Date: February, 2003
Appendix: All Claims on Appeal

Very truly yours,

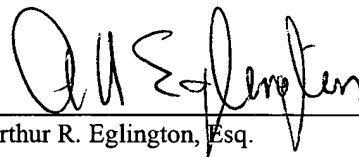


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CERTIFICATE OF MAILING

The undersigned hereby certifies that this MAIN BRIEF ON APPEAL TO THE BOARD CONFORMING WITH 37 C.F.R. §1.192(c) AS AMENDED correspondence is being deposited with the United States Postal Service as First Class Certified Mail in an envelope addressed to: Patent & Trademark Office, Attn: Group 3625, Washington, DC 20231, on February 1, 2003

Date: February 1, 2003



Arthur R. Eglington, Esq.

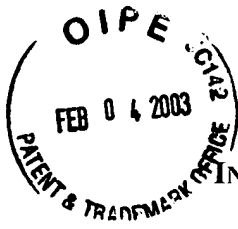
* Cellulitis is inflammation of cellular or connective tissues, which is not CELLULITE, as defined herein. Taber's Medical Dictionary 1981 Ed. pg. 37.

APPENDIX CLEAN COPY OF CLAIMS

1. An oil-in-water emulsion suited for topical application to the skin of a woman evincing the cosmetic condition called cellulite, having the active ingredients comprising:
 - (a) an oil-soluble hydroxyflavone selected from the group consisted of quercetin and fisetin;
 - (b) an oil-soluble isoflavone selected from the group consisting of genistein, diadzein, and biochanin-A;
 - (c) an oil-soluble amino substituted butanoate selected from the group consisting of DL-carnitine, L-carnitine, and carnitine acetate;
 - (d) a water-soluble xanthine selected from the group consisting of theophylline, theophylline salts, caffeine, and theobromine;
 - (e) a water-soluble plant extract *coleus forskohlii*;
 - (f) a solubilizing agent for the oil-soluble ingredients; and,
 - (g) an emulsifying agent for mixing the oil phase with the aqueous phase.
2. The oil-in-water emulsion of Claim 1 wherein quercetin is the hydroxyflavone present in the weight percent of the emulsion volume up to about 5%.
3. The oil-in-water emulsion of Claim 1 wherein fisetin is the hydroxyflavone and is present in the weight volume up to about 5%.
4. The oil-in-water emulsion of Claim 1 wherein the isoflavone is genistein and is present in the weight volume of up to about 5%.
5. The oil-in-water emulsion of Claim 1 wherein the xanthine is theophylline acetate and is present in the weight volume of up to about 4%.

6. The oil-in-water emulsion of Claim 1 wherein the coleus extract is present in the weight volume of up to about 2%.
7. The oil-in-water emulsion of Claim 1 wherein the butanoate is L-acetyl carnitine and is present in the weight volume of up to about 1.5%.
8. The method of treating cellulitis in women wherein the application formulation comprises an oil-in-water emulsion comprising:
 - (a) an oil-soluble hydroxyflavone selected from the group consisted of quercetin and fificetin;
 - (b) an oil-soluble isoflavone selected from the group consisting of genistein, diadzein, and biochanin-A;
 - (c) an oil-soluble amino substitute butanoate selected from the group consisting of DL-carnitine, L-carnitine, and carnitine acetate;
 - (d) a water-soluble xanthine selected from the group consisting of theophylline, theophylline salts, caffeine, and theopromine;
 - (e) a water-soluble plant extract coleus forskohlii;
 - (f) a solubizing agent for the oil-soluble ingredients; and,
 - (g) an emulsifying agent for mixing the oil phase with the aqueous phase.
9. The oil-in-water emulsion of Claim 1 which has been converted to a gel consistency by the incorporation of a natural gum selected from xanthan gum, and carrageenan.
10. The oil-in-water emulsion of Claim 1 which has been converted to a gel consistency by the incorporation of a gelling agent selected from one of methoxycellulose, ethoxycellulose, carboxycellulose, acyanacrylate, polyvinylpyrrolidone, or chitosan.

11. The oil-in-water emulsion of Claim 1 wherein the [bioflavonoid] oligomeric proanthrocyanidins are included as useful in blocking the action of collagenase.



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT EXAMINING OPERATION

GTO H

3 of 3

In re Application of:

PETER T. PUGLIESE

Serial No.: 09/989,019

Filed: November 21, 2001

Title: THE USE OF COMBINED FLAVONES
AND ISOFLAVONES TO TREAT
CELLULITE

Group Art Unit No.: 1617

Supervisory Examiner:

R. Travers (GP 1200)

Phone No.: (703) 308-3627

Examiner: San-Ming Hui

Patent & Trademark Office
ATTN: Group 1617
Washington, D.C. 20231

**MAIN BRIEF TO THE BOARD OF APPEALS CONFORMING
WITH 37 C.F.R. §1.192(c) AS AMENDED 1995**

Sirs:

PREAMBLE

This appeal brief (filed in triplicate with a statutory fee) is being mailed on or about February 1, 2003, and is responsive to the Final Action of the Primary Examiner, mailed 09/10/2002, with a shortened statutory period for our response of three months. Appellant filed a short Rule 116 response on October 3, 2002, rebutting views taken by the Examiner as to the Specification support for certain claims, and concurrently tendering limiting amendments to one claim (#11) of the finally rejected set of claims.

In reply to the PTO Final Action mailed 09/10/02, the Appellant filed the mentioned brief R116 paper, rectifying an informality as to dependent Claim 11, for purposes of claims resolution on appeal. This step called for an advisory action from the PTO as to the tendered claim amendment. Such a PTO advisory has not yet been received, so our submission stands

without objection. Thusly, amended claims form the sole appendix to this Brief on Appeal, reflect the new submission. Also, the of record Rule 132 Declaration of inventor, P.T. Pugliese, forms an integral part of this record on appeal.

This reply settled that the Notice of Appeal due date remained at December 10, 2002. A timely Notice of Appeal was entered on December 10, 2002. The statutory fee is enclosed.

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The of-record sole Applicant, Peter T. Pugliese, Pugliese Group, 4408-B Pottsville Pike, Reading, PA 19605, is the sole party in interest.

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Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. See, e.g., *C.R. Bards, Inc. v. M3 Sys., Inc.* 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998) (describing “teaching or suggestion or motivation [to combine]” as an “essential evidentiary component of an obviousness holding”); *In re Rouffet*, 149 F.3d 1350, 1359, 47 USPQ2d 1453, 1459 (Fed. Cir. 1998) (“the Board must identify specifically . . . the reasons one of ordinary skill in the art would have been motivated to select the references and combine them”); *In re Fritch*, 972 F.3d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (examiner can satisfy burden of obviousness in light of combination “only by showing some objective teaching [leading to the combination]”); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) (evidence of teaching or suggestion “essential” to avoid hindsight); *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 297, 227 USPQ 657, 667 (Fed. Cir. 1985) (district court’s conclusion of obviousness was error when it “did not elucidate any factual teachings, suggestions or incentives from this prior art that showed the propriety of combination”). See also *Graham*,

383 U.S. at 18, 86 S.Ct. 684, 15 L.Ed.2d 545, 148 USPQ at 467 (“strict observance” of factual predicates to obviousness conclusion required). Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor’s disclosure as a blueprint for piecing together the prior art to defeat patentability – the essence of hindsight. *See, e.g., Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed.Cir.1985) (“The invention must be viewed not with the blueprint drawn by the inventor, but in the state of art that existed at the time.”). In this case, the Board fell into the hindsight trap.

We have noted that evidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of the ordinary skill in the art, or, in some cases, from the nature of the problem to be solved, *see Pro-Mold & Tool Co., v. great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed.Cir. 1996), *Para-Ordnance Mfg. v. SGS Importers Intern., Inc.*, 73 F.3d 1085, 1088, 37 USPQ2d 1237, 1240 (Fed.Cir.1995), although “the suggestion more often comes from the teachings of the pertinent references,” *Rouffet*, 149 F.3d at 1355, 47 USPQ2d at 1456. The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular. *Se, e.g., C.R. Bard*, 157 F.3d at 13532, 48 USPQ2d at 1232. Broad conclusory statements regarding the teaching of multiple references, standing alone, are not “evidence.” *E.G., McElmurry v. Arkansas Power & Light co.*, 995 F.2d 1576, 1578, 27 USPQ2d 1129, 1131 (Fed.Cir.1993) (“Mere denials and conclusory statements, however, are not sufficient to establish a genuine issue of material fact.”); *In re Sichert*, 566 F.2d 1154, 1164, 196 USPQ 209, 217, (CCPA 1977) (“The examiner’s conclusory statement that the specification does not teach the best mode of using the invention is unaccompanied by evidence or reasoning and is entirely inadequate to support the rejection.”). In addition to demonstrating the propriety of an obviousness analysis, particular factual findings regarding the suggestion, teaching, or motivation to combine serve a number of important purposes, including: (1) clear explication of the position adopted by the Examiner and the Boards; (2) identification of the factual disputes, if any, between the applicant and the Board; and (3) facilitation of review on appeal. Here, however, the Board did not make particular findings regarding the locus of suggestion, teaching, or motivation to combine the prior art references.

All the obviousness rejections affirmed by the Board resulted from a combination of prior art references, e.g., the conventional trash or yard bags, and the Holiday and Shapiro publications teaching. . .”

* * *

Nor has the Primary Examiner followed the mandate of the CAFC in properly explicating the necessary factual findings so to provide an administrative record showing PTO “evidence”,

on which such findings are based.

A recent panel of the CAFC in *In re Sang-Su Ling* (18 2002) 277 Fed. Report 3d 1338/9, in reversing the BPAI, articulated the settled philosophy of that court on a crucial aspect of patent solicitation and an Examiner invocation of Section 103. In the interest of brevity, only four headnotes (3, 7, 8, and 9) are reproduced below (the full text of that decision is constructively available to the Primary Examiner, or will be supplied by Applicant upon informal request to counsel):

“3. Patents 113(6)

Judicial review of a decision of the Board of Patent Appeals and Interferences denying an application for patent is founded on the obligation of the agency to make the necessary findings and to provide an administrative record showing the evidence on which the findings are based, accompanied by the agency’s reasoning in reaching its conclusions. 5 U.S.C.A. § 103.

7. Patents 111

Analysis of invention by Board of Patent Appeals and Interferences did not comport with either legal requirements for determination of obviousness or with requirements of Administrative Procedure Act (APA) on basis that agency tribunal did not set forth findings and explanations needed for reasoned decisionmaking; examiner used conclusory statements to support this subjective belief that it was obvious that person skilled in the art would have been motivated to combine prior art, and Board rejected need for any specific hint or suggestion in particular reference to support combination of prior art. 5 U.S.C.A. § 706(2); 35 U.S.C.A. § 103.

8. Patents 26(1)

In an obviousness determination, the factual question of motivation to combine prior art is material to patentability, and cannot be resolved on subjective belief and unknown authority. 35 U.S.C.A. § 103.

9. Patents 26(1), 111

In an obviousness determination under patent law, it is improper, in determining whether a person of ordinary skill would have been led to combine references, simply to use that which the inventor taught against its teacher; thus, the Board of Patent Appeals and Interferences must not only assure that the requisite findings are made, based on evidence of record, but must also explain the reasoning by which the findings are deemed to support the agency’s conclusion. 5 U.S.C.A. §

705(2); 35 U.S.C.A. § 103.

SHIFT IN THE EVIDENTIARY BURDEN TO THE PTO PRIMARY EXAMINER

This specification recitation, coupled with the Rule 132 declaration of the sole inventor, has been untenably given short shrift by the Primary Examiner. While the §103 basis of rejection may have been arguable, the of record showings served to overcome any presumption of obviousness, so the final rejection of the invented claims is contrary to patent law standards of the 35 U.S. Code requirements as set forth in §101 and 103.

ARGUMENT REFUTING THE CLAIMS REJECTION PER §103

At the outset, the thrust of the present invention bears repeating. According to the present invention, a treatment protocol for the cosmetic condition in females, commonly known as cellulite, involves novel utilization of the following inter-related physiological precepts. Estrogen can be inhibited by blocking estrogen receptors (ER) located on the fibroblast cells with a selected isoflavone, like genistein. Collagen fibers form a tough fibrous tissue termed the fascia, which hold fatty tissues in discrete compartments. Collagenase breaks down collagen fibers. The action of collagenase can be blocked at the level of collagen by employing proanthocyanidins. The production of estrogen from testosterone can be blocked by another isoflavone like genistein. This isoflavone also blocks the initiation of preadipocytes by estrogen, to form fully-differentiated adipocytes, thus inhibiting the expansion of fat mass. Fat tissue may also be reduced by stimulating the formation of cyclic adenosine triphosphate (cAMP), which cause the activation of lipase on fatty tissue, with coleus forskohlii serving as an effective stimulator of cAMP. The xanthine and theophylline acetate, inhibit the enzymatic action of phosphodiesterase, which destroy a cAMP, thus prolonging the lipase stimulating action of

cAMP. Finally, a cofactor like acetyl carnitine is employed to increase the metabolism of the released free fatty acids by the mitochondria. The protocol is foreign to the citations.

The original 11 claims were rejected under Patent Code §103(a) based on a shotgun (varied) reliance on four U.S. patents Soudant, Majeed, Sekiya, and Koulbanis, two foreign patent documents (Lotte and DeSimone), and two non-patent documents (Kuppusamy and Gennaro), for a total of eight citations.

So, of the six primary citations relied upon by the PTO, only one, Koulbanis '433 even speaks to anti-cellulitis action. Of the two secondary citations, De Simone relates solely to the treatment of cytological disorders, while the Gennaro text teaches that methylcellulose and carrageen are useful jelling agents. So, neither of the secondary citations relate to the treatment of cellulite. The asserted merging of these teachings is classic prohibited hindsight reconstructions.

Broadly, the Examiner has asserted a hindsight reconstruction from scattered citations in seeking to effect a teaching or suggestion of the claimed multicomponent formulation of the present invention. The suggestion to combine elements found in the prior art must come from the Applicant himself, rejections born of hindsight are improper. *Panduit Corp. v. Dennison*, 774 Fed. 2d 1082, 1091-92, (CAFC 1985). It is basic patent law that if a prima facie obviousness, the teachings of references can be combined only if there is some suggestion or incentive to do so. (*ACS Hosp. Sys. v. Montefiore Hospital*, 732 Fd. 1572, 1577 (CAFC 1984).

Also, there must be some reason, suggestion, or motivation found in the prior art, whereby a person of ordinary skill in the field, would make that combination. In re: *Octiker*, 977 Fd. 1443, 1447) CAFC 1992).

In the PTO action of February 14, 2002, pages 3/4, the Examiner notes what elements are common to the present claims that the citations do teach or suggest. In that PTO Action page 4, she concedes that several of the recited elements in the examined claims are neither taught, or let alone suggested. The Applicant will now set forth what other features and motivations that each of the citations lack; and what law precludes the picking and choosing of elements for a proscribed force-fitting of these disparate references in striving to meet the here-claimed recitations.

Soudant '230 teaches a topical emulsion composition containing lipolytic agents, like caffeine and a carnitine, for "slimming." It makes neither a mention of, or suggestion for, use of an isoflavone, a hydroxyflavone, a plant extract that stimulates the action of cyclic AMP, any other bioflavanoids, or capillary protectants, all of which are presently taught and comprise components of the claimed formulation.

While Majeed '596 addresses a method of promoting lean body mass, and treating of a mood disorder by administering internally an effective amount of forskolin, it does not even recognize the distinct biological phenomenon of female cellulite. It surely does not suggest c. forskohlin for inclusion in any topical formulation for treating that cosmetic disorder in women. So there is no motivation or incentive provided here to consider forskoilii in the present setting.

While the Lotte Abstract speaks to lipase inhibitors, containing flavanoid compounds as active agents, to be used in food and drink, only quercetin of the hydroflavones is taught as useful, when combined with McIlvane buffer (a complex oleate and swine spleen lipase), for oral ingestion. Again, there is no mention of human cellulite, or any suggestion of possible utility in a topical, extended term treatment using this hydroxyflavone, inter alia, biochemical compounds.

The Kuppusamy article (1992) is directed to the effects of flavanoids on cyclic AMP and phosphodiesterase on lipids in rat adipocytes. It lists quercetin and fisetin among the 31 flavanoids tested. As to these two flavanoids, they showed a dose-and-time dependent increase in lipolysis which was synergistic with epinephrine. However, there is no teaching here of such flavanoids as being candidate compositions for topical treatment of cellulite, which includes an isoflavone, like genistein or diadzein; and acetyl, L-carnitine to move the fatty acids; a plant extract like coleus F; or other bioflavanoids as capillary protectants. The reference-cited hydroxyflavones are merely two species of the several compounds of the here claimed formulations. They are not remotely suggested for such an anti-cellulite evaluation by the Kuppusamy technical paper.

Sekiya '906 is directed to a method of promoting fat degradation in fat cells by orally, or by injection, of a selected isoflavone to a human subject. The basis for this is solely on in vitro data with preadipocyte (a fat cell precursor). While neither genistein, diadzin or daidzein, or diazeine were tested, and optional with customary inert additives, like bulky agents and excipients included, the selected isoflavones were to be used alone. There is neither a teaching or suggestion here of the use of a topical formulation wherein the hydroxyflavone, a xanthine derivative, and acetyl carnitine, a plant extract like c. Forskohli, and capillary protectant are combined into a useful composition for topical treatment of cellulite. Consequently, while Sekiya is related technology, it lacks any motivation to alter its precise isoflavones so as to be blended with the more complex formulations of the present invention.

Koulbanis '433 is to cosmetic compositions having in combination, a thioether, and a xanthine derivative, applied topically with massage, or by using trans-cutaneous electrophoresis.

The patent is exemplification is limited to caffeine and theophylline, as “an anti-cellulitis” solutions. No other active composition are taught or suggested. The patent is directed to massage or using transcutaneous electrophoresis. As to the “slimming” action, only example VII goes to that, but the recited “cream” formulation employs no enzymes or flavanoids, at all. Cellulitis is not mentioned.

The DeSimone PCT international patent specification teaches the use of L-acetyl carnitines, among other carnatines, for the treatment of cytological disorders related to IGF-I (insulin-like growth factor). This shotgun disclosure is directed to numerous pathologies (see claim 2 for a long list of them), with only obesity having the remotest connection to the female cellulite. Cellulite is, in fact, not mentioned. There is no suggestion of any other active principals, in fact, not of the isoflavones, hydroxyflavones, xanthine, plant extract, and so forth. The reference focuses solely on carnitine derivatives and in no way relates to the formulation of the present invention directed to treatment of cellulite

Lastly, the Examiner would invoke the Gennaro text for the proposition that methyl cellulose and carrageenan are useful as gelling agents, an observation with which Applicant does not take issue. The recitation of these inert ingredients in present dependent claim 9 is not presented as being an independent invention. Rather, it goes to reciting preferred formulations. It is statutory law that these dependent claims incorporate all of the recitations of the independent claims from which they depend.

By way of augmentation of the Specification, in teaching the testing of candidate active entities described in the formulas, a showing from this Applicant under 37 C.F.R. Section 1.68 and 1.132 was submitted. This showing comprises quantifiable clinical evidence that the leading

active components, like genistein, diadzein, and quercetin, when incorporated into topical emulsions will produce an appreciable reduction in fat infiltration, increase connective tissues, and will effect a cosmetic improvement in the appearance of the buttocks.

Looking again to the of-record evidence of Appellant, there is the undisputed recitation of Specification pages 12 and 13, also of the Rule 132 Declaration of P.T. Pugliese. From the bar charts of that Declaration, it is clear that the lead compound (genistein) is capable of inhibiting the undesirable destructive effects of estrogen on connective tissue. Genistein is representative of the three-member Markush Group of main Claim 1. Utility has been shown for this novel formulation. Unexpected results here are absolutely not called for under the patent statute.

The Examiner's allegation that it would have been obvious when the invention was made to employ all the active compounds together in one composition or method is simply untenable. Most of this citation is focused on narrowed human conditions, if at all, or teach only one or two active principles for a clinical effect. To meet even the terms of the oil-in-water emulsion of claim 1 for topical use, the Examiner has resorted to at least four different publications, each of which does not provide a motivation for it's dissection and reconstitution in a novel context.

Indeed, it can be argued that certain of these citations teach away from the present formulations, which thus undermines prima facie obviousness. Cf. *In re: Sponnable*, 405 Fd 2d 578, 587 (CCPA 1969). A reference teaches a way when a person of ordinary skill would be led in direction divergent from that of the path taken by the Applicant here.

By way of example, Soudant, Majeed, Lotte, Sekiya, and DeSimone are all directed to treatments for other human problems, like the varied manifestations of obesity. None, save

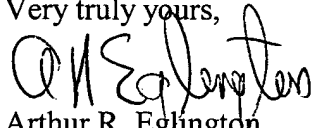
Koulbanis, even speak to anti-cellulitis action.*

The contrived cutting and pasting of the several citations is untenable in the law, and should be withdrawn upon fresh reconsideration in light of these extended remarks.

Lastly, the enclosed Rule 132 Declaration establishes that representative flavones are capable of inhibiting the undesirable destructive effects of estrogen on connective tissue and thus provide a positive effect on treating cellulite, not cellulitis.

The allowance of the agreeably amended set of original claims 1-11, is courteously solicited.

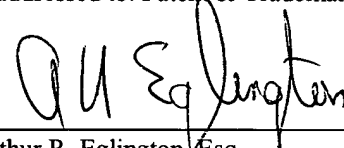
Date: February, 2003
Appendix: All Claims on Appeal

Very truly yours,

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CERTIFICATE OF MAILING

The undersigned hereby certifies that this MAIN BRIEF ON APPEAL TO THE BOARD CONFORMING WITH 37 C.F.R. §1.192(c) AS AMENDED correspondence is being deposited with the United States Postal Service as First Class Certified Mail in an envelope addressed to: Patent & Trademark Office, Attn: Group 3625, Washington, DC 20231, on February 1, 2003

Date: February 1, 2003



Arthur R. Eglington, Esq.

* Cellulitis is inflammation of cellular or connective tissues, which is not CELLULITE, as defined herein.
Taber's Medical Dictionary 1981 Ed. pg. 37.

APPENDIX CLEAN COPY OF CLAIMS

1. An oil-in-water emulsion suited for topical application to the skin of a woman evincing the cosmetic condition called cellulite, having the active ingredients comprising:

(a) an oil-soluble hydroxyflavone selected from the group consisted of quercetin and fisetin;

(b) an oil-soluble isoflavone selected from the group consisting of genistein, diadzein, and biochanin-A;

(c) an oil-soluble amino substituted butanoate selected from the group consisting of DL-carnitine, L-carnitine, and carnitine acetate;

(d) a water-soluble xanthine selected from the group consisting of theophylline, theophylline salts, caffeine, and theobromine;

(e) a water-soluble plant extract *coleus forskohlii*;

(f) a solubilizing agent for the oil-soluble ingredients; and,

(g) an emulsifying agent for mixing the oil phase with the aqueous phase.

2. The oil-in-water emulsion of Claim 1 wherein quercetin is the hydroxyflavone present in the weight percent of the emulsion volume up to about 5%.

3. The oil-in-water emulsion of Claim 1 wherein fisetin is the hydroxyflavone and is present in the weight volume up to about 5%.

4. The oil-in-water emulsion of Claim 1 wherein the isoflavone is genistein and is present in the weight volume of up to about 5%.

5. The oil-in-water emulsion of Claim 1 wherein the xanthine is theophylline acetate and is present in the weight volume of up to about 4%.

6. The oil-in-water emulsion of Claim 1 wherein the coleus extract is present in the weight volume of up to about 2%.
7. The oil-in-water emulsion of Claim 1 wherein the butanoate is L-acetyl carnitine and is present in the weight volume of up to about 1.5%.
8. The method of treating cellulitis in women wherein the application formulation comprises an oil-in-water emulsion comprising:
 - (a) an oil-soluble hydroxyflavone selected from the group consisted of quercetin and fifeletin;
 - (b) an oil-soluble isoflavone selected from the group consisting of genistein, diadzein, and biochanin-A;
 - (c) an oil-soluble amino substitute butanoate selected from the group consisting of DL-carnitine, L-carnitine, and carnitine acetate;
 - (d) a water-soluble xanthine selected from the group consisting of theophylline, theophylline salts, caffeine, and theopromine;
 - (e) a water-soluble plant extract coleus forskohlii;
 - (f) a solubizing agent for the oil-soluble ingredients; and,
 - (g) an emulsifying agent for mixing the oil phase with the aqueous phase.
9. The oil-in-water emulsion of Claim 1 which has been converted to a gel consistency by the incorporation of a natural gum selected from xanthan gum, and carrageenan.
10. The oil-in-water emulsion of Claim 1 which has been converted to a gel consistency by the incorporation of a gelling agent selected from one of methoxycellulose, ethoxycellulose, carboxycellulose, acyanacrylate, polyvinylpyrrolidone, or chitosan.

11. The oil-in-water emulsion of Claim 1 wherein the [bioflavonoid] oligomeric proanthrocyanidins are included as useful in blocking the action of collagenase.